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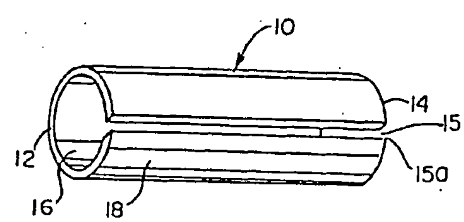
(54) Title: DRUG DELIVERY DEVICE FOR STENT

(57) Abstract

A device adapted for mounting on a stent, the device comprising a sheath being made of polymeric material that includes drugs such as pharmaceutical agent(s) or radioactive agent(s) for delivery to an implant site. The sheath includes a main body of a generally tubular shape, and may include mounting means for attaching same to the stent. The device may have a slit therein, and may comprise a helical coil, a cylinder or any other suitable shape or design which fits a particular stent. The sheath may include a coating or coatings thereon containing drugs, surgical adhesives or a combination thereof.



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Description

DRUG DELIVERY DEVICE FOR STENT

BACKGROUND OF THE INVENTION

This invention relates to a device for providing mechanical support to a vessel lumen of a living being. This invention also relates to the delivery of materials which prevent restenosis of a vessel.

A variety of medical situations requires the use of a mechanism to expand and support a constricted vessel and to maintain an open passageway through the vessel. A few examples of such situations following angioplasty include holding a dissection in place, preventing closure during spasm, and preventing acute closure due to thrombosis. In these situations, devices, commonly known as stents, are useful to maintain the patency of body passages, to prevent stenosis of a dilated vessel, to eliminate the danger of occlusion caused by "flaps" resulting from intimal tears that may be associated with angioplasty, or to hold two ends of a vessel in place.

Stents are generally tubular in configuration, open ended and are expandable between a generally unexpanded insertion diameter and an expanded implantation diameter. Stents are commonly placed or implanted by a mechanical transluminal procedure.

Specifically, U.S. Patent 4,733,665 to Palmaz discloses a number of stent configurations for implantation with the aid of a catheter. U.S. Patent 5,019,090 to Pinchuk discloses a generally cylindrical stent and technique for implanting it using a deflated balloon catheter to position the stent. U.S. Patents 4,503,569 to Dotter and 4,512,338 to Balko et al. disclose a spring stent and a shape memory alloy stent. There are also self-expanding stents such as those described in U.S. Patents 4,732,152 to Wallsten et al. and 4,848,343 to Wallsten et al. All of these patents are hereby incorporated by reference.

Stents have been made using materials of varied composition and conformation. McGreevy et al U.S. Patents 4,690,684 and 4,770,176 describe a meltable stent that is inserted into the interior of the ends of a blood vessel during anastomosis. Anastomosis refers to the surgical or physical connection of two tubular structures, such as veins or arteries. The stent is made of blood plasma, which is biologically compatible with the living being and which melts rapidly in response to heat.

Fischell et al., in U.S. Patent 4,768,507 describe an intravascular stent which is an unrestrained coil spring having an outside diameter of 2 to 12 millimeters and a length of 5 to 25 millimeters. The materials of construction are stainless steel, and a

titanium alloy. Decreased thrombogenicity is achievable by coating the outside of the coil with a non-thrombogenic material such as ULTI carbon.

Leeven et al., in U.S. Patent 4,820,298 describe a stent having a flexible tubular body made from a thermal plastic to the form of a helix. Polyester and polycarbonate copolymers are selected as particularly desirable materials.

Wolff et al., in U.S. Patent 4,830,003 describe a stent made from wires formed into a cylinder. The wires are made of a biocompatible metal. Biocompatible metals include 300 series stainless steels such as 316 LSS, as well as platinum and platinum-iridium alloys, cobalt-chromium alloys such as MP35N, and unalloyed titanium.

Wiktor in U.S. Patent 4,886,062 describes a stent made from low memory metal such as a copper alloy, titanium, or gold. The stent is preformed into a two-dimensional zig-zag form creating a flat expandable band.

Gianturco in U.S. Patent 4,907,336 describes a wire stent having a cylindrical shape that results from an expandable serpentine configuration. Malleable materials of construction are preferably included from the group of annealed stainless steels, tungsten and platinum.

Goldberg et al, in Canadian Application 2,025,626, describes a bio-degradable infusion stent used to treat ureteral obstructions. The application describes an extruded material of construction made of epsilon-caprolactone (15-25% w/w of terpolymer composition); glycoside (5-50% w/w) and L(-)lactide (45-85% w/w). This material was described as having a minimum tensile strength of at least 500 pounds per square inch, preferably 650 psi; elongation of greater than 10%, preferably greater than 100%; and Shore A hardness equal to 50-100%, preferably 75-95%. The Goldberg et al patent application describes a method for incorporating radiopaque materials such as barium sulfate into the polymer in amounts ranging from 5-30%. The mechanism of biodegradation is described as hydrolysis resulting in degradable products excreted in urine or reabsorbed into tissues. The duration of functional life of the stent is estimated at about 3-7 weeks.

Wilcoff in U.S. Patent 4,990,155 describes a plastic stent having an inherently expandable coil conformation. The "inherency" results from an elastic memory conferred by electron beam radiation imparting cross-linkages that provide an inherent tendency to return to a given diameter after any distortion. Matcrials of construction

include high density polyethylene. Optionally, this material is compounded with an anti-coagulant and/or an x-ray opaque material such as bismuth-sub-carbonate.

Sigwart, Canadian Patent Application 2,008,312, describes a stent made from a malleable flat sheet having a reticulated pattern. The reticulated pattern includes non-deformable squares or diamonds. The stent is made by rolling the sheet and locking the sheet into a spiral having a small diameter. The sheet is locked into a spiral by a tie interwoven into the reticulated pattern. Once inserted into the lumen of a vessel, the spiral is expanded and held in place by flaps integrated into the outer body of the stent.

Shockley et al., in U.S. Patent 4,994,033, describe a drug delivery dilatation catheter having three flexible, plastic tubes concentrically arranged relative to each other. The outermost sleeve of this catheter contains microholes for drug delivery. These microholes are made with a laser beam. Drugs that can be delivered by this system include aspirin, persantin, heparin, and prostaglandins. Drugs are delivered when externally applied pressure causes the innermost sleeve to balloon out. The drug is then forced through the microholes to spray and to treat a lesion.

There are also stents which deliver agents or drugs to blood passing through the vein or artery that are generally beneficial to the recipient. In addition, stents can deliver drugs or biologically active agents at a controlled rate to blood passing through the vessel lumen as well as to the vessel wall. Silvestrini in U.S. Patent 5,234,456 describes a hydrophilic stent comprising a wall structure where at least a portion thereof is a hollow wall in which a hydrophilic material for drug delivery is placed. U.S. Patent 5,443,458 to Eury et al., is directed to a multilayer laminated resorbable stent having a structural layer and additional layers stated to release drugs at predictable rates. Froix in U.S. 5,258,020 describes a self-restrained stent with an elastic memory, the stent optionally being formulated to provide for drug administration.

It is known that when stents are expanded to their implantation diameter the ends of the stent may press into the vessel or cavity walls, especially the distal end of the stent. The sharp or pointed edges and ends of some stents may then damage the walls. Once damage has occurred, there is a likelihood that restenosis will occur at these points where the stents ends and edges have penetrated or pressed against the walls.

Restenosis occurs in a number of cases where a stent has been used. Tearing of the wall of the passage or injury of the endothelial cell layer are possible causes of the

restenosis. The torn wall or flap usually is the source of the blockage. When the wall is torn, a flap of tissue is created, which falls into the passage and blocks it. It is then necessary to perform another procedure to remove the blockage and generally, another stent is needed to open the vessel or other passage. Metal stents are known to cause 10% to 30% or more restenosis in application.

Therefore, it desirable to utilize a stent which reduces the chances of a damaged vessel wall or body passage which leads to further problems and further necessary procedures. However, current stents are not designed to reduce the occurrence of cutting of vascular passages or the like.

U.S. Patent Application No. 09/072,944, incorporated herein by reference, is directed to a stent having at least one smooth end. The stent may include a coating or coatings on one or both end portions to provide a smooth finish to reduce possible damage to body passages when the stent is deployed and delivered. The stent may also contain drugs or surgical adhesives or a combination thereof in or on the coated portion of the stent. The stent may also be of the type where the materials of the stent may be treated to have a smooth flexible end or ends. The stent may also be of a configuration such that at least one end is more flexible than the middle portion of the stent.

U.S. Patent Application No. 08/874,190, incorporated herein by reference, discloses a polymeric layered stent characterized in that it includes a multilayered material comprised of an inner polymer layer and an overlying outer polymer layer. The self-expanding or balloon expandable stent disclosed therein is provided in two forms, one including inner and outer polymeric layers, and another comprising a prior art stent provided with polymeric layer(s) coated thereon.

While U.S. Applications 09/072,944 and 08/874,190 are directed in part to this need, there still exists a need for a means for delivering drugs or biologically active agents which assist in preventing restenosis, which can be easily mounted on an existing stent prior to implantation.

SUMMARY OF THE INVENTION

Accordingly, it is an object of the present invention is to provide a polymeric device adapted for mounting onto a stent. The device of polymeric material may comprise a sheath or sleeve that is cylindrical, a helical coil, or any other suitable shape or design which fits a particular stent. The stent may be metallic or non-metallic, or alternatively a

combination of metallic and non-metallic materials. An example of a preferred stent for use with the device of the present invention is the NIR stent, set forth in U.S. Patent 5,733,303, incorporated herein by reference. In addition, the device may be used with a stent as set forth in U.S. Application No. 08/874,190, incorporated herein by reference.

The device may be of a biocompatible material and may be either biodegradable or non-biodegradable. The device may also be water soluble. It may contain pharmaceutical agent(s) or radioactive agent(s). The device is adapted for mounting onto a stent prior to use for insertion into a lumen of a vessel in a living being, and may be expanded with the stent. The device is optionally biodegradable, and may be made from at least one biodegradable material that is also biocompatible and includes a drug which is released into the lumen of the vessel at a rate controlled by the rate of degradation of the biodegradable material.

Generally, any prior art stent may be improved by providing it with the device of the present invention. The use of this inventive device with an existing stent provides a simple method for reducing restenosis.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is an enlarged perspective view of a device according to the present invention;

Figures 2a and 2b are perspective views of an alternative embodiment of the device of the present invention;

Figure 3 is a perspective view of an alternaive embodiment of the device of the present invention;

Figure 4 is a perspective view of an alternative embodiment of the device of the present invention;

Figure 5 is a cross section taken along the line 5-5 of Figure 4;

Figure 6 is a perspective view of an alternative embodiment of a device according to the present invention;

Figure 7 is a cross section taken along line 7-7 of Figure 6;

Figure 8 is a perspective view of an alternative embodiment of a device according to the present invention;

Figure 9 is a fragmentary perspective view of the sheath as shown in Figure 8 mounted on a stent;

Figure 10 is a fragementary perspective view as in Figure 9 showing the stent and sheath after expansion of the stent; and

Figure 11 is a fragementary side elevational view with parts broken away of the stent with the sheath of the present invention in an implanted site.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention is a polymeric device adapted for mounting onto a stent. Referring to Figures 1-4, the device may be a sheath as shown generally at 10. Sheath 10 has a proximal end 12, a distal end 14, an interior surface 16 and an exterior surface 18.

As shown at Figures 2a, 2b and 3, sheath 10 may have a slit 15 therein extending from proximal end 12 to distal end 14. As shown at Figure 2a, slit 15 is a longitudinal slit 15a. Figure 2b shows the same sheath in a compressed configuration it may take on prior to being mounted on a stent. Alternatively, slit 15 may be a helical slit 15b, as shown at Figure 3.

Referring to Figure 4, sheath 10 may be provided with perforations 17 therethrough. In addition, sheath 10 may comprise multiple layers, for example as shown in cross section at Figure 5 having two layers. Alternatively, sheath 10 may comprise a plurality of layers. Referring to Figures 6-7, sheath 10 may be shaped like a spring, which spring may optionally be formed from a tubular member, as exemplified by the cross section at Figure 7.

Referring now to Figures 8-10, a sheath comprising a helical coil is shown. Figure 8 is a perspective view of sheath 10. At Figure 9, a partial section view of sheath 10 mounted on a stent 20 is shown prior to implantation and expansion. Stent 20 includes a generally tubular main body 21, a proximal end 22 (not shown in this view), a distal end 24 (not shown in this view), an interior surface 26 and an exterior surface 28. Prior to implantation, sheath 10 is mounted on stent 20 such that the exterior surface 28 of main body 21 faces the interior surface 16 of sheath 10.

In use, sheath 10 is placed on the outer surface 24 of stent 20 prior to implantation thereof. Sheath 10 may be held on stent 20 by any suitable means including compressive force, glue, a protective sheath, socks or the like.

The compressive force may be supplied by the sheath itself, the stent or both. The glue is preferably a biocompatible glue such as fibrin, collagen or gelatin. Any

appropriate bioadhesive may be used. For example, the following bioadhesives may be used singly or in combination:

cyanoacrylate: ethyl cyanoacrylate, butyl cyanoacrylate, octyl cyanoacrylate, hexyl cyanoacrylate;

fibrin glue: fibrinogen/thrombin/Factor XIII/calcium as catalyst

gelatin-resorcinol-formol (GRF) glue: formed from gelatin, resorcinol and water in the presence of formaldehyde, glutaraldehyde and heat (45°C);

mussel adhesive protein, prolamine gel and transforming growth factor beta(TGF-B);

polyacrylic acid, modified hydrocellulose, hydroxypropylmethyl cellulose, hydroxypropylcellulose, carboxymethyl cellulose, sodium alginate, gelatin, pectin, polyvinylpylindone, polyethylene glycol, aldehyde relative multifunctional chemicals, polyallylsaccharose, and polypeptides.

A protective sheath may also be used to secure sheath 10 to stent 20. A sheath or sheaths as disclosed in U.S. Application Nos. 08/812,351 and 09/034,434, incorporated herein by reference, may be used, but would be retained over sheath 10 in use.

At least one sock covering a portion of sheath 10 over stent 20 may also be used. Such a retaining device as is disclosed in U.S. Application No. 08/917,027, incorporated herein by reference, may be used.

One use of the sheath of the present invention is to allow physicians to add it to any stent and delivery system they already have. The sheath may therefore be provided as a stand alone device.

Stent 20 with sheath 10 mounted thereto is positioned at the inner surface wall 34 of the vessel 32 by radially compressing the stent with sheath to a tubular diameter less than the diameter of the vessel 32 and moving stent 20 to a desired site within vessel 32. Stent 20 is implanted in the known manner depending upon its type. For example, a self expanding stent would be released from compression so that the stent can radially spring out to abut against the inner surface wall 34 of vessel 32. The stent may also be of the balloon expandable type. In any case, sheath 10 is adapted for mounting onto stent 20 and expansion therewith. Figure 10 shows sheath 10 after expansion of stent 20.

At Figure 11, sheath 10 and stent 20 are shown in an implanted site, in the lumen 30 of a tubular vessel 32 in a body. Upon implantation, the exterior surface 18 of

sheath 10 faces an inner surface wall 34 of the vessel 32. Stent 20 provides mechanical support to tubular vessel 32 in a living being. The stent strengthens the area of vessel 32 in which it is implanted. Sheath 10 releases a pharmaceutical agent or radioactive agent into lumen 30 of tubular vessel 32. The rate of release may vary.

The present invention may be used with any stent. Such a stent may range from 1 millimeter in diameter to 50 millimeters in diameter and from 1 millimeter in length to 50 millimeters in length. The size of the stent is dictated by the lumen of the vessel to which the stent is placed. Tubular main body 21 suitably has a length of up to approximately 5 centimeters.

Sheath 10 may be of any size suitable for use with a stent being implanted.

Many suitable materials may be used to form the sheath 10 of the present invention. For example, hydrophilic polymers, copolymers (block or graft) or their cross-linked versions (e.g. hydrogels), may be used, the polymers including poly(hydroxyethyl methacrylate) and derivatives; poly(vinyl alcohol); polyethylene oxide; poly(propylene oxide); polyacrylamides; polyacrylic acid; polymethacrylic acid; poly(N-vinyl-2-pyrollidone); hydrophilic polyurethanes; poly(amino acid); water soluble cellulosic polymers (sodium carboxymethyl cellulose, hydroxyethyl cellulose, for example); collagens; carrageenan; alginate; starch; dextrin; and gelatins.

The device of the present invention may be made of biodegradable polymers including poly(lactide); poly(glycolide); polydioxanone(PDS); polycaprolactone; polyhydroxybutyrate(PHBT); poly(phosphazene); poly(phosphate ester); poly(lactide-co-glycolide); poly(glycolide-co-trimethylene carbonate); poly(glycolide-co-caprolactone); polyanhydrides; collagen or other connective proteins or natural materials, hyaluronic acid, adhesive proteins, co-polymers of these materials as well as composites or combinations thereof and combinations of other biodegradable polymers.

In addition, the device of the present invention may be made of biodegradable materials that are also biocompatible. By biodegradable is meant that a material will undergo breakdown or decomposition into harmless compounds as part of a normal biological process. The device may also include bioactive agents which permit endothelial cells to grow on the device and the stent. It is believed that the endothelial cell growth will encapsulate particles of the stent during biodegradation that would otherwise come loose and form emboli in the blood stream.

Suitable biodegradable materials for the device of the present invention include polylactic acid, polyglycolic acid, collagen or other connective proteins or natural materials, polycaprolactone, hyaluronic acid, adhesive proteins, co-polymers of these materials as well as composites and combinations thereof, and combinations of other biodegradable polymers. Biodegradable glass or bioactive glass is also a suitable biodegradable material for use in the present invention. Preferably the materials have been accepted by the U.S. Food and Drug Administration.

One advantage of using a variety of biodegradable materials within the sheath is control of degradation. Biodegradable materials degrade at different rates, ranging from days or weeks to several years. Consequently, the presence of different biodegradable materials in the stent permits the sheath to degrade in a predictable manner. The device may further be coated with a biodegradable film layer.

Where sheath 10 is of a biodegradable material, the rate of release of the pharmaceutical agent or radioactive agent will be controlled by the rate of degradation of the biodegradable materials.

Further, the device of the present invention may be made of nonbiodegradable biocompatible materials such as polytetrafluoroethylene(PTFE); polyurethanes; polyamides; polyesters; polyethers; polyketones; polyether ester elastomers; polyether amide elastomers; polyacrylate-based elastomers; polyethylene; and polypropylene.

These lists are exemplary only. Any appropriate material may be used.

The sheath of the present invention includes pharmaceutical agent(s) and/or radioactive agent(s) or other biologically active materials. Where the sheath is biodegradable, these drugs, pharmaceutical agents, radioactive agents or biologically active materials are contained within the biodegradable materials of which the stent is composed. As the sheath biodegrades, drugs are released into the surrounding tissue or to the bloodstream. Thus, the rate of drug release is controlled by the rate of degradation of the biodegradable materials. A material that degrades rapidly will release the drug faster than a material that degrades slowly.

Drugs are incorporated into the biodegradable sheath using techniques known in the art. The techniques include simple mixing or solubilizing with polymer

solutions, dispersing into the biodegradable polymer during the formation of the sheath, or coating onto an already formed sheath.

Where the sheath has a film added thereto, drugs can be incorporated into the film by methods such as melting or solvation. Alternatively, biologically active agents are incorporated into the film layer by entrapment between such layer and the surface of biodegradable material sandwiched together, thereby further promoting release of the drugs or agents in a controllable manner.

The drugs or other biologically active materials incorporated into the sheath of the present invention perform a variety of functions. The functions include but are not limited to an anti-clotting or anti-platelet function and preventing smooth muscle cell growth on the inner surface of the vessel to reduce the chance of in-stent restenosis. The drugs include but are not limited to drugs that inhibit or control the formation of thrombus or thrombolytics such as heparin or heparin fragments, aspirin, coumadin, tissue plasminogen activator (TPA), urokinase, hirudin, and streptokinase, antiproliferatives (methotrexate, cisplatin, 5-fluorouracil, Taxol, Adriamycin, and the like) antioxidants (ascorbic acid, carotene, B, vitamin E, and the like), antimetabolites, thromboxane inhibitors, non-steroidal and steroidal antiinflammatory drugs, Beta and Calcium channel blockers, genetic materials including DNA and RNA fragments, and complete expression genes, carbohydrates, and proteins including but not limited to antibodies (monoclonal and polyclonal) lymphokines and growth factors, prostaglandins, and leukotrienes. The sheath material may also incorporate bioactive materials such as fibronectin, laminin, elastin, collagen, and intergrins. Fibronectin, for example, promotes adherence of the sheath to the tissue of the vessel 32.

In one specific example of a biodegradable material incorporating drugs, a poly-L-lactide having an intrinsic viscosity of 2.3 dl/g is used to form monofilament fibers using a spin or melt spinning process. Five percent aspirin or 5% heparin was incorporated into the melt of the poly-L-lactide prior to fiber formation. The fibers formed had a diameter of approximately 0.5 millimeters. The monofilaments were then stretched under temperatures ranging from 50° C to 200° C to orient the fiber. The temperature employed depends upon the kind of material used to make the fiber. The final diameter of the oriented fiber falls within a range of 0.1 to 0.3 millimeters. Similar processing was used to incorporate 5% aspirin or 5% heparin into poly-L-lactide and polyglycolide.

The device of the present invention may also include bioadhesives to be delivered to the site where the stent is needed. It is known that bioadhesives can be used to repair tissue walls. It is therefore desirable to utilize a polymer to deliver a bioadhesive to the stent implantation location. In this manner, a potential problem could be averted by the presence of the bioadhesive in the case of a tear or dissection.

Just as the use of a variety of biodegradable materials facilitates a controlled degradation of a biodegradable sheath according to the present invention, so similarly does the incorporation of a variety of drugs into the biodegradable materials facilitate control of drug release to perform a variety of functions. For instance, drugs released from the outer surface as the outer surface degrades facilitate adherence of the sheath to the inner surface wall 34 of the vessel 32. Drugs released from fibers perform a variety of functions, ranging from promoting cell growth to altering the blood clotting mechanisms, depending upon what drug released. In one embodiment, drugs released from the sheath as it degrades may temper platelet function in blood flowing through lumen .

The device of the present invention may also be used as a drug delivery system to prevent restenosis or for other treatment. The drugs may include radioactive materials to irradiate and prohibit smooth muscle cell growth. Angioplasty and stent deployment may cause injury of the endothelial cell layer of blood vessels, causing smooth muscle cell proliferation, leading to restenosis. By accelerated endothelialization on the inner wall surface of vessels will prevent or prohibit the smooth muscle growth. To stimulate endothelialization without provoking smooth muscle cell proliferation, specific growth factors may be included and delivered. Growth factors include vascular endothelial growth factor (VEGF), transforming growth factor beta (TGFβ), insulin growth factor-1 (IGF-1), platelet derived growth factor (PDGF), basic fibroblast growth factor (bFGF), etc.

All such materials are referred to herein generally as "drugs" or therapeutics. These drugs may be dispersed in the matrix of the polymeric material.

For carrying drugs, a gel-like material may be used. The sleeve may be comprised of such a material, or it may be applied over the sleeve as a coating. There are several ways to apply drugs to such materials. The first way is to mix the drug with the materials, then form a sleeve therefrom. Alternatively the mixture may coated onto a sleeve. The gel-like materials can be cast as film or sheet with drug together, then formed into a sleeve or laminated to a sleeve.

Another way is to form a sleeve from a gel-like material without a drug, or to coat or laminate a polymeric sleeve with a gel-like material without the drug. The sleeve is made, and then sterilized. Due to the gel-like nature, the sleeve can then be inserted into a drug solution. The drug will be absorbed into/onto the gel.

The resulting drug-carrying sleeve can then be mounted to a stent and delivered into the body. The drug will then be released.

In one embodiment of the invention, the sleeve may be made of polyethylene oxide containing Taxol or coated with such a material. Other materials that may be used are copolymers such as PGA/PLA, PEO/PLA or the like containing a drug such as Taxol or heparin.

Preferred gel- like materials for use as a drug delivery sleeve or coating for a stent when drug delivery is desired are polyethylene oxide, polyvinyl pyrollidone, polyacrylates, and their blends or copolymers or lightly cross linked forms. Polyethylene glycol block copolymer with polylactides or other polyesters are examples. Hydrophilic polyurethane, poly(maleic anhydride-alt-ethylene) and their derivatives are examples. Other materials are polysaccharides and their derivatives. There are also sodium alginate, karaya gum, gelatin, guar gum, agar, algin carrageenans, pectin, locust bean gums, xanthan, starch-based gums, hydroxy alkyl and ethyl ethers of cellulose, sodium carboxymethyl cellulose. Some of the materials will be heated, then cooled, then a gel is formed. Some of the above are food gels. Some of them are bioadhesives.

Any drugs may be used, singly or in combination. For example, the drugs can be an anticoagulant, e.g. aspirin, ticlopidine, an RGD peptide-containing compound, heparin, antithrombin compounds, platelet receptor antagonists, antibodies, urokinase, prostaglandin inhibitors, platelet inhibitors, or antiplatelet peptide. The drug can be an inhibitor of vascular cell growth, DNA, RNA, cholesterol-lowering agents, vasodilating agents. The drug can be any drug such as Taxol, 5-fluorouracil, Beta-Estradiol, Tranilast, Trapidil, Probucol, Angiopeptin or any combination of them.

Since there are many drugs and many polymers, the sleeve can have multiple layers of different polymers with the same or different drugs. For example, the sleeve can have two layers of the same polymer with one layer with drug and another layer without drugs. The sleeve may have two layers of the same polymer with two different drugs as another example.

In particular, various combinations of a cycling sinase inhibitor identified as p21 and the vascular endothelial growth factor identified as VEGF, an endothelial nitrogen, may preferably be included in and dispensed from the sleeve or coating provided thereon.

Incorporation of drugs and growth factors into the sleeve material or coating thereof can also be performed by several other methods, including the solvent method, melting method, soaking method and spraying method. If both polymer and drug have a cosolvent, a solution case will be an easy way to provide the polymer matrix loaded with the drug or growth factor. If the polymer can be melted at low temperature and the drug or growth factor tolerates heating, a melting method can be used to mix the drug or growth factor into the polymer matrix. Also, a polymer-drug solution or suspension solution can be used for coating to provide a layer containing the drug or growth factor.

In another embodiment of the invention the sleeve may be coated with a film of bioadhesive. Bioadhesives glue the tissue together. Using a bioadhesive for the coating serves two purposes. If a tear has occurred prior to or during delivery of the stent on which the sleeve is mounted, the tissue can be repaired. In this manner, blood flow will be maintained in a vessel, for example. The bioadhesive may or may not also have drugs loaded for delivery. Dissection, cutting or tearing occurs in some stent delivery and PTCA procedures. Bioadhesives or surgical adhesives may be used to repair the passage wall. However, these tears or cuts are not necessarily discovered immediately. In those cases, a further medical procedure must be undertaken to repair the wall. The need for such an additional medical procedure may be eliminated where a bioadhesive is included as a coating on the sleeve mounted to the stent which is deployed in place, as the bioadhesive will repair damage to the vessel wall. The bioadhesive is chosen as the coating for the sleeve, or is used in addition to a coating on the sleeve and is applied in a known manner to the sleeve. The end or edge, side, outside and/or inside of the sleeve may utilize the bioadhesive.

Any appropriate bioadhesive may be used. For example, the following bioadhesives may be used singly or in combination:

cyanoacrylate: ethyl cyanoacrylate, butyl cyanoacrylate, octyl cyanoacrylate, hexyl cyanoacrylate;

fibrin glue: fibrinogen/thrombin/Factor XIII/calcium as catalyst

gelatin-resorcinol-formol (GRF) glue: formed from gelatin, resorcinol and water in the presence of formaldehyde, glutaraldehyde and heat (45°C);

mussel adhesive protein, prolamine gel and transforming growth factor beta(TGF-B);

polyacrylic acid, modified hydrocellulose, hydroxypropylmethyl cellulose, hydroxypropylcellulose, carboxymethyl cellulose, sodium alginate, gelatin, pectin, polyvinylpylindone, polyethylene glycol, aldehyde relative multifunctional chemicals, polyallylsaccharose, and polypeptides.

Suitable materials for the device of the present invention and suitable drugs to be delivered thereby are also set forth in U.S. Application No. 08/874,190.

Although the present invention has been described with reference to preferred embodiments, workers skilled in the art will recognize that changes may be made in form and detail without departing from the spirit and scope of the invention.

The above Examples and disclosure are intended to be illustrative and not exhaustive. These examples and description will suggest many variations and alternatives to one of ordinary skill in this art. All these alternatives and variations are intended to be included within the scope of the attached claims. Those familiar with the art may recognize other equivalents to the specific embodiments described herein which equivalents are also intended to be encompassed by the claims attached hereto.

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Claims

WHAT IS CLAIMED IS:

What is claimed is:

1. An implantable intraluminal apparatus comprising in combination:

an expandable intraluminal stent comprising a main body portion having a first end portion, a second end portion, a middle portion, an exterior surface and an interior flow passage defined therethrough; and

a sheath constructed and arranged for mounting on the stent for delivery of drugs to an implanted site, said sheath comprising a biocompatible polymeric material and a drug carried thereby.

2. The apparatus of claim 1 wherein the sheath comprises polyurethane.

3. The apparatus of claim 1 wherein the sheath comprises polytetrafluoroethylene.

4. The apparatus of claim 1 wherein the sheath comprises a gel-like material.

5. The apparatus of claim 1 wherein the sheath comprises a cellulose polymer.

6. The apparatus of claim 1 wherein the sheath comprises a biodegradable polymer.

7. The apparatus of claim 1 wherein the sheath comprises poly(N-vinyl-2-pyrollidone).

8. The apparatus of claim 1 wherein the sheath comprises polyethylene oxide.

9. The apparatus of claim 1 wherein the drug is selected from the group consisting of pharmaceutical agents, radioactive agents, bioactive agents and combinations thereof.

11. The apparatus of claim 1 wherein the drug is selected from the group consisting of TAXOL, vascular endothelial growth factor, heparin, 5-fluorouracil, beta-estradiol, tranilast, trapidil, probucol, and angiopeptin.

12. The apparatus of claim 1 wherein the sheath is cylindrical.

13. The apparatus of claim 1 wherein the sheath further comprises a proximal end, a distal end and a slit extending from the proximal end to the distal end.

14. The apparatus of claim 13 wherein the slit is a longitudinal slit.

15. The apparatus of claim 13 wherein the slit is helical.

16. The apparatus of claim 1 wherein the sheath is a helical coil.

17. The apparatus of claim 1 wherein the sheath comprises a plurality of layers.

18. The apparatus of claim 17 wherein the plurality of layers is comprised of the same material.

19. The apparatus of claim 17 wherein the plurality of layers is comprised of different materials.

20. The apparatus of claim 17 wherein at least one of the layers includes a drug.

21. The apparatus of claim 1 wherein the sheath further comprises an inner surface, an outer surface, and a coating covering at least a portion of the outer surface thereof.

22. The apparatus of claim 21 wherein the coating comprises a biocompatible polymer.

23. The apparatus of claim 21 wherein the coating comprises polyethylene oxide.

24. The apparatus of claim 21 wherein the coating comprises polyurethane.

25. The apparatus of claim 21 wherein the coating comprises a gel-like material.

26. The apparatus of claim 21 wherein the drug is carried by the coating.

27. The apparatus of claim 21 wherein the coating includes a bioadhesive.

28. The apparatus of claim 27 wherein the bioadhesive is selected from the group consisting of cyanoacrylate, fibrin glue, gelatin-resorcinol-formol glue.

29. The apparatus of claim 21 wherein the coating comprises a plurality of layers.

30. The apparatus of claim 29 wherein the plurality of layers is comprised of the same coating material.

31. The apparatus of claim 29 wherein the plurality of layers is comprised of different coating materials.

32. The apparatus of claim 29 wherein at least one of the layers includes a drug.

33. An implantable intraluminal apparatus comprising:

a sheath constructed and arranged for mounting on a stent for delivery of drugs to an implanted site, said sheath comprising a biocompatible polymeric material and a drug carried thereby.

34. A sheath constructed and arranged for mounting on a stent for delivery of drugs to an implanted site, said sheath comprising a biocompatible polymeric material and a drug carried thereby.

35. A sheath for an implantable intraluminal apparatus for delivery of a stent, the sheath constructed and arranged for mounting on a stent for delivery of drugs to an implanted site, said sheath comprising a biocompatible polymeric material and a drug carried thereby.

36. A sheath for being delivery into the body with a stent, the sheath constructed and arranged for mounting on a stent for delivery of drugs to an implanted site, said sheath comprising a biocompatible polymeric material and a drug carried thereby.

37. A drug delivery sheath for delivering drugs within the body, the sheath constructed and arranged for being associated with a stent for delivery of drugs to an implanted site, said sheath comprising a biocompatible polymeric material and a drug carried thereby.

38. A sheath constructed and arranged for being introduced within the body for delivery of drugs to an implanted site, said sheath comprising a biocompatible polymeric material and a drug carried thereby.

Fig. 1

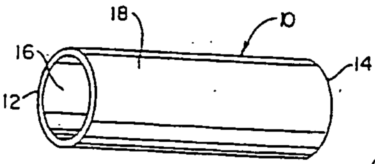


Fig. 2a

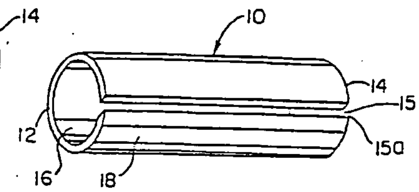


Fig. 7

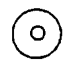


Fig. 3

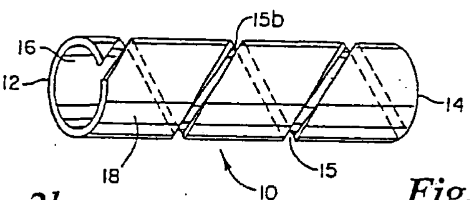


Fig. 2b

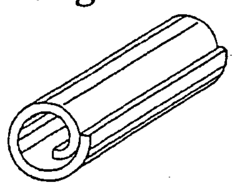


Fig. 4

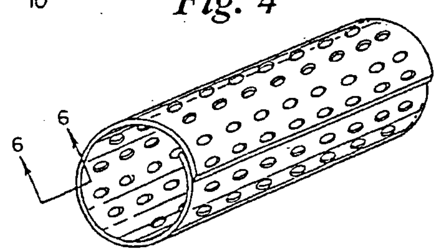


Fig. 5

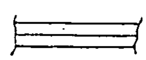


Fig. 6

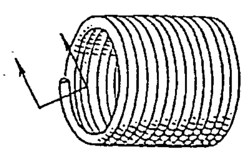


Fig. 8

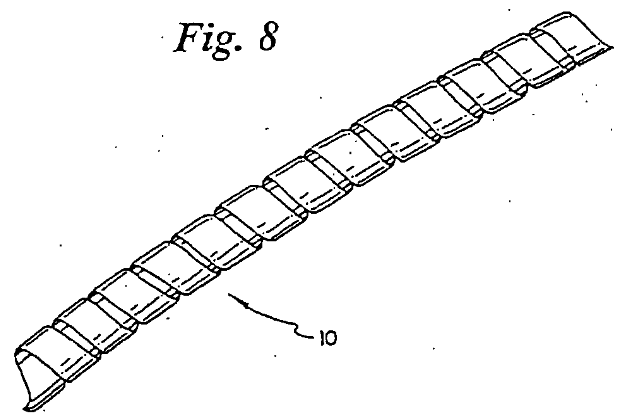


Fig. 9

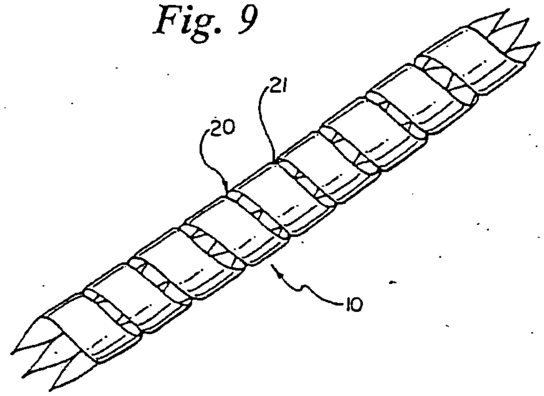


Fig. 10

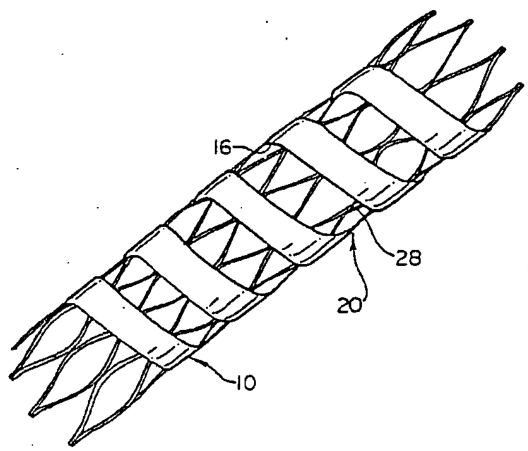
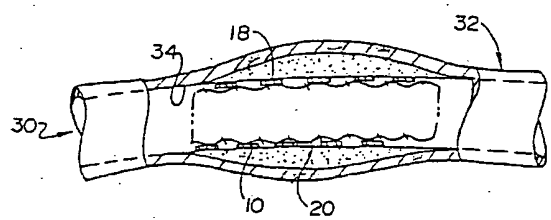


Fig. 11



INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/19697

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61L31/08 A61L31/16 A61L31/18 A61K51/12 A61F2/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61L A61K A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 January 2000	25/01/2000
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer ESPINOSA, M

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International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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X	WO 98 36784 A (COOK INC) 27 August 1998 (1998-08-27) claims	1
A	WO 93 06792 A (SCIMED LIFE SYSTEMS INC) 15 April 1993 (1993-04-15) figures	1-38

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